### (19) 世界知的所有権機関 国際事務局



# 

(43) 国際公開日 2004 年10 月7 日 (07.10.2004)

PCT

### (10) 国際公開番号 WO 2004/085653 A1

(51) 国際特許分類<sup>7</sup>: C12N 15/62, C12P 21/02, C07K 19/00, 14/44, 14/47, A61K 38/16, A61P 35/00

(21) 国際出願番号:

РСТ/JP2004/003956

(22) 国際出願日:

2004年3月23日(23.03.2004)

(25) 国際出願の言語:

日本語

(26) 国際公開の言語:

日本語

(30) 優先権データ: 特願2003-081337 2003年3月24日(24.03.2003) J

(71) 出願人 (米国を除く全ての指定国について): 学校法人 日本医科大学 (NIPPON MEDICAL SCHOOL FOUN-DATION) [JP/JP]; 〒1138602 東京都文京区千駄木 1 丁 目 1 番 5 号 Tokyo (JP).

(72) 発明者; および

(75) 発明者/出願人 (米国についてのみ): 太田成男 (OHTA, Shigeo) [JP/JP]; 〒1138602 東京都文京区千駄木 1 丁目 1 番 5 号 日本医科大学内 Tokyo (JP). 麻生 定光 (ASOH, Sadamitsu) [JP/JP]; 〒1138602 東京都文京区 千駄木 1 丁目 1番 5 号 日本医科大学内 Tokyo (JP).

(74) 代理人: 平木 祐輔 , 外(HIRAKI, Yusuke et al.); 〒 1050001 東京都港区虎ノ門一丁目17番1号 虎ノ門5森 ビル 3階 Tokyo (JP).

(81) 指定国 (表示のない限り、全ての種類の国内保護が可能): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) 指定国 (表示のない限り、全ての種類の広域保護が可能): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), ユーラシア (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), ヨーロッパ (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### 添付公開書類:

一 国際調査報告書

2文字コード及び他の略語については、定期発行される各PCTガゼットの巻頭に掲載されている「コードと略語のガイダンスノート」を参照。

(54) Title: CELL DEATH-INDUCING FUSED GENE ACTING SPECIFICALLY ON CANCER AND GENE PRODUCT THEREOF

(54) 発明の名称: 癌に特異的に作用する細胞死誘導融合遺伝子及びその遺伝子産物

(57) Abstract: It is intended to provide a protein having a potent effect of inducing cell death (i.e., a fused protein having a denatured Bax protein carrying GEP fused to the N-terminal and a homing signal peptide having a homing effect on cancer cells further fused in the N-terminal side); a gene encoding the fused protein; and a cancer cell proliferation inhibitor containing the fused protein. Namely, a fused gene containing a cell death-inducing gene specifically acting on cancer cells, which is a fused gene having a gene encoding a cancer cell-specific homing signal peptide sequence, a gene encoding a green fluorescent protein (GFP) and a gene encoding Δ-NBax with a deletion of the N-terminal sequence containing BH3 region of human Bax in this order, and a fused protein encoded by the fused gene.

「(57) 要約: 本発明は、強力な細胞死誘導作用を有するタンパク質、すなわちGFPをN末端に融合した改変型Baxタンパク質のN末端側にさらに癌細胞へのホーミング作用を有するホーミングシグナルペプチドを融合させた融合タンパク質、該融合タンパク質をコードする遺伝子、および該融合タンパク質を含む癌細胞増殖抑制剤を提供する。本発明は、癌細胞に特異的に作用する細胞死誘導遺伝子を含む融合遺伝子であって、癌細胞に特異的なホーミングシグナルペプチド配列をコードする遺伝子、グリーン蛍光タンパク質(GFP)をコードする遺伝子およびヒトBaxのBH3領域を含むN末端配列を除去したΔNBaxをコードする遺伝子をこの順番で融合させた融合遺伝子および該融合

## PATENT COOPERATION TREATY

### PCT

### NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 26 May 2004 (26 05 2004) From the INTERNATIONAL BUREAU

HIRAKI, Yusuke

Toranomon No.5 Mori Building Third

Floor

17-1, Toranomon 1-chome Minato-ku, Tokyo 105-0001

Japan



1	20 May 2004 (20.03.2004)	<u>να</u> Γ †Ωζίτι
L		VAC:
	Applicant's or agent's file reference PH-2011-PCT	IMPORTANT NOTIFICATION
	, and a second of the second o	

International application No. International filing date (day/month/year) PCT/JP2004/003956 23 March 2004 (23.03.2004)

International publication date (day/month/year) Priority date (day/month/year) Not yet published 24 March 2003 (24.03.2003)

Applicant

### NIPPON MEDICAL SCHOOL FOUNDATION et al

- By means of this Form, which replaces any previously issued notification concerning submission or transmittal of priority documents, the applicant is hereby notified of the date of receipt by the International Bureau of the priority document(s) relating to all earlier application(s) whose priority is claimed. Unless otherwise indicated by the letters "NR", in the right-hand column or by an asterisk appearing next to a date of receipt, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- (If applicable) The letters "NR" appearing in the right-hand column denote a priority document which, on the date of mailing of this Form, had not yet been received by the International Bureau under Rule 17.1(a) or (b). Where, under Rule 17.1(a), the priority document must be submitted by the applicant to the receiving Office or the International Bureau, but the applicant fails to submit the priority document within the applicable time limit under that Rule, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- 3. (If applicable) An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b) (the priority document was received after the time limit prescribed in Rule 17.1(a) or the request to prepare and transmit the priority document was submitted to the receiving Office after the applicable time limit under Rule 17.1(b)). Even though the priority document was not furnished in compliance with Rule 17.1(a) or (b), the International Bureau will nevertheless transmit a copy of the document to the designated Offices, for their consideration. In case such a copy is not accepted by the designated Office as priority document, Rule 17.1(c) provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date Priority application No. Country or regional Office or PCT receiving Office

Date of receipt of priority document

24 Marc 2003 (24.03.2003) / 2003-081337

JP.

13 May 2004 (13.05.2004)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Farid ABBOU (Fax 338 7010)

Facsimile No. (41-22) 338.70.10

Form PCT/IB/304 (January 2004)

Telephone No. (41-22) 338 8169